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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,228	09/29/2003	Samir M. Hanash	31755-A-PCT-USA-I	1891

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ARENT FOX PLLC
1675 BROADWAY
NEW YORK, NY 10019

EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	

MAIL DATE	DELIVERY MODE
08/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/674,228	HANASH ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, and 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/10/2007 has been entered.

2. Claim 1 has been amended and claim 3 has been cancelled.

3. Claims 1, 2, and 4 are currently pending and under consideration.

Rejections Maintained

Claim Rejections - 35 USC § 103

4. Claims 1, 2, and 4 remain rejected under 35 USC 103 for the reasons previously set forth in section 6, pages 4-8 of the Office Action of February 12, 2007.

Applicants argue that the examiner's maintained rejection is in error. Hirsch et al. clearly discounts the value of a 2D-gel separation for identifying proteins to which a patient with cancer raises autoantibodies, as compared to an individual without cancer. Careful examination of Hirsch at al. clearly shows that Hirsch et al. actually teaches away from the current invention. In reviewing the 2D Western blots of figures and 3, Hirsch et al. conclude that other than the spots at 65kDa, all other staining was 'the usual background" i.e. of no value as information concerning the discovery and identification of proteins to which patients with cancer raise autoantibodies, in so doing it is clear that Hirsch et al. do not disclose the currently claimed invention and provide no guidance to one of skill in the art as to how to arrive at it. Applicants

argue that Hirsch et al. positively discourage such a skilled person to even try by teaching that any spots unrelated to proteins previously discovered by 1D Western blot are merely "the usual background".

Applicants' argument has been considered, but has not been found persuasive because it is well within the skill of those of ordinary skill in the art to recognize background noise in their experimental work by comparing the results of the test assay with the control assay and the detection of background would not discourage one of skill in the art in the art from performing the prior art method. Hirsch et al. successfully detected a protein that is reactive to autoantibodies in the serum of patients with Hodgkin's disease, thus one of skill in the art would be motivated with a reasonable expectation of success to two-dimensional electrophoresis to identify cellular protein antigens to which a cancer patient produces autoantibodies. Furthermore, a review of Hirsch et al. did not reveal a teaching that any spots unrelated to proteins previously discovered by 1D Western blot are merely "the usual background".

Applicants argue that the examiner asserts that the teaching of Hirsch et al., must be combined with that of Krska et al. and the two publications taken as a whole. In the first case the Applicants respectfully suggest that there is no such guidance in Hirsch et al. or Krska et al. to consult the other, and that, since these two studies are in completely unrelated fields, they do not represent the same art. Moreover, even taken together they fail to teach or suggest the presently claimed invention.

Applicants' arguments have been considered, but have not been found persuasive because the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention

must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In particular, Hirsch et al., teach a method of identifying proteins that induce autoantibodies in Hodgkin's disease which is a form of cancer, i.e. lymphoma, comprising the steps of isolating proteins from L428 cancer cells derived from Hodgkin's disease cancer patients, followed by subjecting isolated proteins to two-dimensional PAGE, followed by Western blot analysis with sera from cancer patients as compared to sera from normal control patients, wherein the proteins bound by antibodies present in the cancer patients serum but not the normal control serum are identified as proteins to which a subject with cancer produces autoantibodies, and detecting the proteins to which the autoantibodies in the subject's serum sample have bound with an antibody that is specific for autoantibody in the subjects sample. The teaching drawn to a method consisting-in-part of 2-D electrophoresis is further validated and suggested by Krska et al who teach the conventional 2-D electrophoresis method of detecting primary antibody bound to the antigen of interest for detection of proteins in 2D gel electrophoresis transferred to a membrane. Thus, the combined references provide not only the means, but also the motivation to make the claimed invention, that is to identify protein to which a subject with cancer produces autoantibodies as set forth in claims 1, 2, and 4 and the invention is obvious for the reasons of record.

Applicants argue that even assuming arguendo that the skilled person looking to find better ways of identifying proteins to which a patient with cancer would raise antibodies would consider the field of bacterial evolution of the Dnak protein and characterization of a monoclonal antibody thereto, she would still not have arrived at the present invention.

Applicants argue that Krska et al. is concerned with characterizing a monoclonal antibody raised against an exogenous antigen. This is completely unrelated to the production of antibodies against an autologus protein, as is the case in Hirsch et al. and which only looks at 1D separation as in the current invention in which 2D separation is used to identify cellular antigens to which a cancer patient raises autoantibodies. It is well understood in the field of immunology that the mammalin immune system is designed to act against exogenous (non-self) antigens. Conversely, there should be no response to autologous (self) antigens which are generally ignored by the immune system. Where antibodies" are raised to autoantigens, the individual normally suffers from an autoimmune disease, such as rheumatoid arthritis, scarlet fever or lupus.

Applicants argue that in oncology, it is believed that an autoimununne response is triggered by abnormal expression and/or excretion and proteolysis of self proteins which are then rendered antigenic. The problem to be solved was how to identify these newly created self antigens and provide them a ready means for diagnosing cancer based on detection of autoantibodies to them in individuals as provided in the present invention.

Applicants argue that thus a combination of Krska et al. and Hirsch et al. fails to provide such a method or suggest such a method based on the 2D Western blotting of unknown proteins screened with sera containing unknown antibodies, in Hirsch et al. a priori knowledge of the target protein is required from a 1D Western blot before perform a 2D Western blot, and any staining of spots inconsistent with the prior identified antigen are specifically discounted as background. Krska et al. is silent on the level of background staining and so provides no further guidance that a priori knowledge of the antigen is required. To the contrary, Krska et al. requires

absolute knowledge of the target antigen, since it must first be used to immunize BALB/c mice or New Zealand white rabbits to provide the sera for use in in Western blotting.

Applicants' arguments have been carefully considered, but have not been found persuasive. In regard to the biology of the immune system, Applicants are arguing limitations not found in the claims. Although Krska et al. is not drawn to the identification of proteins bound by cancer autoantibodies, Krska et al. teach the routine and conventional method at the time the invention was made of using 2D gels and Western blotting to identify a protein of interest bound by an antibody comprising using a signal-generating component bound to a second antibody that is specific for the primary antibodies used initially. The combined references teach a method for identifying proteins, to which a subject produces autoantibodies consisting of the claimed method using the 2D electrophoresis and the steps/limitations of claims 1, 2, and 4 wherein the combined references do not require a priori identification of the protein in order to determine protein differences. Furthermore, one of skill in the art could easily identify the cellular protein antigens to which autoantibodies react by simple repetition of the experiment which is routinely done in the art without any a priori knowledge of the protein to be identified. Thus, for the reasons previously set forth and above, one of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Hirsch et al. and Krska et al. to perform the instantly claimed method.

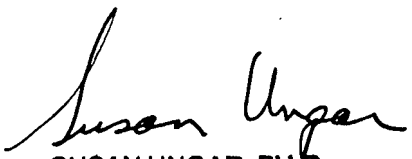
Applicant's arguments have not been found persuasive and the rejection is maintained.

5. No claims allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Peter J. Reddig
Examiner
Art Unit 1642

PJR